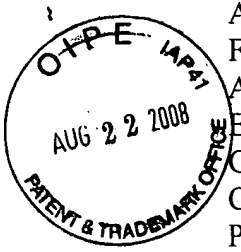


Application Number 10/625,100
Filing Date 07-22-2003
Application Type: Utility
Examiner: Ton, Thaian N
Group Art Unit 1632
Class/Sub-Class 436/366
Publication No"US2005-0019907 A1
Publication Date 01-27-2005
Inventor Santiago Munne
Address of inventor: 3 Regent Street, Livingston, NJ-07039. Tel 201-386-8962
Title: Obtaining normal disomic stem cells from chromosomally abnormal embryos

8/21/2008

**Pro Se Inventor's Reply to the Final Office Action of March 5, 2008**

Dear Examiner Thaian Ton,
As a pro se inventor, it is my understanding that if you find any patentable material you can write the claim for me. Please find my responses to your Final Office action of March 5, 2008.

Claim rejections:

Claims 7-8 -35 USC 112

Examiner suggests that the specification "while being enabling for methods of producing disomic human embryonic cell lines" is not enabling for making "stem cell lines".
The specification incorporates several articles and patents that teach to "any person skilled in the art" of making stem cells. Patent specification need only describe and show possession of the invention in its totality and not teach (hybridtech v Monoclonal antibody inc 231U.S.P.Q.81 (federal circuit 1986)), herself, states that Thompson patents and reference's teach how to make stem cells from "normal" non trisomically derived disomic embryonic cells. "Thomson et al ...teach the specific art-recognized" What Thompson did not teach, nor anticipate, is that trisomic cell lines can revert to "normal" disomic cell lines. In re Edwards, 568 F 2d at 1351, 196 U.S.P.Q.2d at 468 the Court held that the detailed disclosure of the process and possible reactants were sufficient to provide a "written description" of one of the possible products of that reaction. And, In re Ruschig 54 CCPA 1551, 154 USPQ 118 (CCPA 1967) that a sufficient disclosure is "one that marks a trial through the woods by supplying blaze marks on the trees". We believe we have marked a clear trail to making stem cells from trisomically derived disomic embryonic cell lines.

Examiner brings in a new ground of rejection which is the Wanda factors. We quote from sections of In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). In Wands, the

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Court held that the specification was enabling with respect to the claims at issue and found that "there was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the application was filed;" and "all of the methods needed to practice the invention were well known." After considering all the factors related to the enablement issue, the court concluded that "it would not require undue experimentation to obtain antibodies needed to practice the claimed invention."
This clearly falls under the Wanda factors, but the Examiner's interpretation fails to note that obtaining an antibody for a stem cell such as TRA-1-60, SSEA-1, SSEA-3, SSEA-4, TRA 1-81, OCT 4 or akaline phosphatase does not require undue experimentation. In fact, these antibodies are commercially available and testing these disomic with said antibodies also does not require undue experimentation. Therefore, under Wanda testing for epitopes to structurally define the trisomically derived disomic cells which are stem cells does not require undue experimentation. The claim breadth, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, the amount of experimentation are all satisfied by simply identifying even one stem cell epitope on one cell of a population of trisomically derived disomic cells. This can be done by using one antibody such as TRA-1-60 to see if any cells in the population of trisomically derived disomics bind said antibody or a mimic thereof.
In the micrograph below, we show just such a population of cells binding a TRA-1-60 rhodamine-labeled peptide mimic of TRA-1-60 binding antibody. This did not require undue experimentation in that it only required adding said rhodamine peptide mimic of TRA-1-60 to the slide and viewing said population under a fluorescence microscope. The very bright cells are the trisomically derived disomic stem cells binding the TRA-1-60 ligand mimic. The dark cells are the non-binding differentiating cells. Anyone skilled in the art could repeat this simple procedure. It is just a matter of adding 1 microliter of stain to the sample and viewing same.
I have attached a notarized affidavit from Sasha Sadowy attesting to her ability to reproduce and enable the procedures and methods outlined in the application and to achieve similar if not identical results. Sasha Sadowy is a licensed embryologist and is of "ordinary-skill in the arts" in making and identifying stem cell lines.
This evidence should address your new 35 USC 112 para 1 enablement objections to claims 7 and 8.
**We have now included in the IDS an article by Lavon et al. precisely reproducing our published methods, in which they test for all the antibodies, karyotyping and differentiating function thereby meeting examiner's rejections. The Lavon et al.**

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**paper follows our published patent application and our publication Munne et al. (2005) Fertil Steril 84:1328-1334 which was included in the prior IDS, and incorporated as part of the specifications.**

**Responding to point 2 of page 6 of the final action, once a cell line is classified as a stem cell line its use is well known in the art. The Lavon et al. paper did not require any separation of normal from trisomic since at the end most cells were disomic. If it was necessary, once the disomic fraction is large, subcloning should eliminate any trisomic cells.**

Claim Rejection of 35 USC112

We amend the claim 7 as:
Claim 7 (Currently amended) I claim the method of producing disomic cell lines comprising the steps of:

a) culturing trisomic embryos onto mouse feeder cells consisting of mouse embryonic fibroblast cells (ATCC-STO) said mouse embryonic fibroblast cells having been previously mitotically inactivated by mitomycin [[mitocimin]] C in gelatin-tissue culture dishes; and,

b) maintaining said mouse feeder cells **using maintenance medium comprising** [medium] Dulbecco's Modified Eagle Medium (DMEM) without sodium pyruvate, glucose 4500 mgL-1 supplemented with 20% fetal bovine serum, 0.1 mM -mercaptoethanol, 1% non-essential amino acids, 1 mM L-glutamine, 50 units ml L-1 penicillin; and,

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c) supplementing said **maintenance** medium with human recombinant Leukemia Inhibitory factor at 2000 units mL-1 and bFGF 4 ng/ml; and,

d) culturing said embryos in said **supplemented maintenance** medium until day 12; and,

e) fixing and analyzing by FISH said **disomic** [embryonic] cell lines, and identifying and isolating disomic cell lines within said trisomic embryos wherein disomic cell lines are produced.

Claim Rejection of 35 USC102
Regarding the creation of uniparental stem cell lines we are still in the process of demonstrating this point.
Thompson did not do uniparental studies on the origin of their stem cell lines in their patent or publications. We believe our stem cell lines will have the characteristics of stem cell lines but be unique in that they are uniparental.

Your consideration of this RCE application and amendment is requested and appreciated.

Sincerely,

Santiago Munne